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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/918,637	08/01/2001	Ahmed Jehanli	01246.0134	2644

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EXAMINER	
HINES, JANA A	

ART UNIT	PAPER NUMBER
1645	

DATE MAILED: 02/07/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/918,637	JEHANLI ET AL.	
	Examiner	Art Unit	
	Ja-Na Hines	1645	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *21 November 2005*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *24-38* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *24-38* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Amendment Entry

1. The amendment filed November 21, 2005 has been entered. Claims 1-23 have been cancelled. Claims 24-38 are under consideration in the office action.

Withdrawal of Rejections

2. The following rejections have been withdrawn in view of applicants' amendments and arguments:

a) The rejection of claims 1-4,6,7, 9, 12, 14-15 under 35 U.S.C. 102(b) as being anticipated by de Jaeger et al., (US Patent 4,837,168 published June 6, 1989);

b) The rejection of claims 1-3, 5-7, 9,12, 14-16 and 19-21 under 35 U.S.C. 103(a) as being unpatentable over Jehanli et al., (1996) and Cole et al., (US Patent 4,589,612) in view of Maggio (1987);

c) The rejection of claims 8 and 22-23 under 35 U.S.C. 103(a) as being unpatentable over de Jaeger et al., (US Patent 4,837,168) and Jehanli et al., (1996) as applied to claims 1-2 and 6-7 above, further in view of Baker et al., (US Patent 5,624,806 published April 1997).

New Grounds of Rejection

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

3. Claims 24-30 and 32-35 are rejected under 35 U.S.C. 102(b) as being anticipated by de Jaeger et al., (US Patent 4,837,168). The claims are drawn to a method for the qualitative or quantitative determination of a drug in a biological fluid, comprising the steps of : I) providing a first part coated with a drug conjugate wherein said first part consists of a stick; ii) adding the biological fluid to a second part which contains a labeled antidrug antibody being the specific binding partner of the drug conjugate and is adapted for receiving biological fluid, wherein said labeled antidrug antibody is labeled with gold material or latex particles; iii) bringing said first part into contact with the biological fluid in said second part for the qualitative and quantitative determination of the drug in the fluid; iv) removing said first part from said second part after a predetermined period of time; and v) determining a color change of said first part indicating the qualitative or quantitative determination of the drug in the biological fluid. The dependant claims are drawn to specific drug conjugates, particle materials and materials and shapes of the first and second parts.

de Jaeger et al., teach a method of qualitatively or quantitatively determining a component of a complex formed between at least one specific binding protein and its

corresponding bindable substance (col. 2, lines 20-25). de Jaeger et al., teach the visualization of immunocomplexes using gold colloidal metal particles wherein specific techniques are referred to as sol particle immunoassays (col. 1, lines 54-65). de Jaeger et al., also teach detecting colored or colorable latex particles as being convenient and simple (col. 12, lines 63-66). The color signal is easily detected and optionally quantified either directly or if necessary after development (col. 2, lines 40-43). The optical properties of latex particles especially their color characteristics make them optimal labels (col. 2, lines 50-56). Examples of colored or colorable latex particles are well known in the art (col. 3-5, lines 10-40). de Jaeger et al., teach labeling one component of the complex with colored latex particles (col. 2, lines 27-39). The bindable substance to be detected is immobilized on an appropriate immobilizing solid support prior to its complexing with the labeled binding proteins, which are specific to the bindable substance (col.11-12, lines 67-5). In many cases, the specific binding proteins will be antibodies to specific antigens or haptens (col. 13, lines 15-17). The bindable substances which can be detected includes peptides, hormones, vitamins, polysaccharides, pharmacological agents and any other molecules for a specific binding counterpart exists in biological systems or that can be synthesized (col. 13, lines 58-64). Hapten analytes include the general class of drugs, hormones, vitamins, antimicrobial drugs and antibiotic drugs, steroids such as cortisol which is a corticosteroid, cardiac glycoside drugs, and a wide variety of other drugs (col. 14-15, lines 22-56). Thereby teaching that any drug including a wide variety of antimicrobials and psycho-pharmaceutical agents are encompassed by de Jaeger et al. The immobilizing supports

can be made of a variety of polymeric materials or nitrocellulose and may take any convenient form such as dip-stick (col. 12, lines 12-20). Thereby teaching a drug conjugate coated stick made of the same instantly claimed surface material. Example 1 teaches the preparation of latex bound antibodies (col. 17, lines 60-19). Example 2 teaches the design of a dipstick test in undiluted human serum (col. 19-21, lines 33-15). The immobilization procedures recite that bovine serum albumin was used to conjugate the drug and coat it onto the dipstick paper (col. 20, lines 27-39). The performance of the test recites that the dipstick was immersed into a mixture containing antibody coupled to colored latex beads, thus a container which could hold a dipstick held the labeled antibody solution thereby meeting the limitations of the claims (col. 20, lines 55-68). de Jaeger et al., teach homogenous determinations using art known procedures such as competitive binding techniques (col. 11, lines 5-8).

Thus, de Jaeger et al., teach a method for the qualitative or quantitative determination of a drug in a biological fluid, comprising the steps of: I) providing a first part coated with a drug conjugate wherein said first part consists of a stick; ii) adding the biological fluid to a second part which contains a labeled antidrug antibody being the specific binding partner of the drug conjugate and is adapted for receiving biological fluid, wherein said labeled antidrug antibody is labeled with gold material or latex particles; iii) bringing said first part into contact with the biological fluid in said second part for the qualitative and quantitative determination of the drug in the fluid; iv) removing said first part from said second part after a predetermined period of time; and v) determining a color change of said first part indicating the qualitative or quantitative

determination of the drug in the biological fluid. de Jaeger et al., also teach the specific drug conjugates, particle materials and materials and shapes of the first and second parts, just as required by the instant claims.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

4. Claims 31 and 36-38 are rejected under 35 U.S.C. 103(a) as being unpatentable over de Jaeger et al., (US Patent 4,837,168), Jehanli et al., and Baker et al. (US Patent 5,624,806).

The claims are drawn to a method for the qualitative or quantitative determination of a drug in a biological fluid, comprising the steps of: i) providing a first part coated with a drug conjugate wherein said first part consists of a stick; ii) adding the biological fluid to a second part which contains a labeled antidrug antibody being the specific binding partner of the drug conjugate and is adapted for receiving biological fluid, wherein said labeled antidrug antibody is labeled with gold material or latex particles; iii) bringing said first part into contact with the biological fluid in said second part for the qualitative and quantitative determination of the drug in the fluid; iv) removing said first part from said second part after a predetermined period of time; and v) determining a color change of said first part indicating the qualitative or quantitative determination of the drug in the

biological fluid. The dependant claims are drawn to specific drug conjugates, particle materials and materials and shapes of the first and second parts.

de Jaeger et al., (US Patent 4,837,168) have been discussed above, however de Jaeger et al., do not teach a lisinopril-rabbit serum albumin drug conjugate.
Jehanli et al., (1996) teach determination of Captopril, an orally active angiotension-converting enzyme drug, in human blood by an ELISA assay. The quantitation of captopril in biological fluids has been carried out previously in the art, however the author describes the development of a sensitive, simple and rapid ELISA assay for the determination of captopril (page 914). Preparation of rabbit serum albumin (RSA)-captopril conjugate for the immunoassay was disclosed again teaches a drug conjugate (page 915). Thus making a drug conjugate as described by the claims to be between a drug and a protein. The microtitre strips were coated with the RSA-captopril (page 915). Anti-captopril antibody was added to the tube shaped wells and strips (page 915); thereby teaching a second part that contains labeled antibody and is adapted for receiving biological fluid. Color development was terminated after 30 minutes (page 915). Human plasma samples containing various concentrations of the drug were tested and amounts of captopril were qualitatively or quantitatively determined (page 915). Jehanli et al., teach a methods for qualitative or quantitative determination of a drug in a biological fluid comprising a first stick shaped part coated with a drug conjugate and a second tube-shaped part that contains a labeled antibody and is adapted for receiving biological fluid such as plasma wherein the first and second parts are contacted to

indicate by color change the drug activity or presence. However Jehanli et al., do not teach the lisinopril as the drug conjugated to rabbit serum albumin.

Baker et al., teach antibodies to cardiac hypertrophy factors and their uses. Baker et al., teach that ACE inhibitors are angiotension-converting enzyme inhibiting drugs which prevent the conversion of angiotension I to angiotension II (col. 15 lines 47-50). ACE inhibitors that both prevent the conversion of angiotension I to angiotension II include the peptide drugs known as such as captopril and lisinopril (col. 15 lines 55-57). Thus Baker et al., teach the antigen lisinopril along with antibodies to lisinopril.

It would have been prima facie obvious to modify the method for qualitative or quantitative determination of a drug in a biological fluid comprising a first part coated with a drug conjugate and a second part that contains a labeled antibody as taught by de Jaeger et al., and exchange the drug conjugate and labeled antibody to be lisinopril conjugated to rabbit serum albumin and anti-lisinopril antibody as taught by Jehanli et al., and Baker et al. No more than routine skill would have been required to exchange the conjugated captopril for a conjugated lisinopril when Baker et al., teach that these drugs are alternative and functionally equivalent drugs and no more than routine skill is required to exchange these drugs. One would have a reasonable expectation of success by incorporating the ACE drug lisinopril, when the prior art already teaches the determination of another ACE related drug which has similar functions in the method of de Jaeger et al., and Jehanli et al., which already teach using the labeled antibodies to qualitatively or quantitatively determine the presence of a drug in a biological fluid.

Response to Arguments

5. Applicant's arguments filed November 21, 2005 have been fully considered. The examiner notes that the rejection of claims 8 and 22-23 under 35 U.S.C. 103(a) as being unpatentable over de Jaeger et al., Jehanli et al., (1996) and Baker et al., (US Patent 5,624,806) has been withdrawn. However, because the same references have been used in the new 35 U.S.C. 103(a) rejection applicants' arguments will be addressed below.

Applicants' assert that the present invention is drawn to the detection of a drug conducted by means of a competition between the drug in the biological fluid and the drug conjugate immobilized on the first part. However, contrary to applicants' assertions, de Jaeger et al., clearly disclose competitive assay formats. Applicants also assert that de Jaeger et al., does not disclose the use of particles like applicant does. However the claims state that the particles are used to label the anti-drug antibody, and de Jaeger et al., teach labeling the antibody with the particles. Moreover, in response to applicant's argument that de Jaeger et al., does not disclose the use of particles like applicant does, the fact that applicant has recognized another advantage which would flow naturally from following the suggestion of the prior art cannot be the basis for patentability when the differences would otherwise be obvious. See *Ex parte Obiaya*, 227 USPQ 58, 60 (Bd. Pat. App. & Inter. 1985). Therefore applicants' arguments are not persuasive and the rejection is maintained.

Applicants' urge that Baker et al., does not cure the deficiencies of the rejection and the combination of references do not establish a *prima facie* case of obviousness.

In response to applicant's argument, the examiner recognizes that obviousness can only be established by combining or modifying the teachings of the prior art to produce the claimed invention where there is some teaching, suggestion, or motivation to do so found either in the references themselves or in the knowledge generally available to one of ordinary skill in the art. See *In re Fine*, 837 F.2d 1071, 5 USPQ2d 1596 (Fed. Cir. 1988) and *In re Jones*, 958 F.2d 347, 21 USPQ2d 1941 (Fed. Cir. 1992). In this case, the references teach providing a first stick part coated with a drug conjugate; an addition step; bringing said first part into contact with the biological fluid in said second part for the qualitative and quantitative determination of the drug in the fluid; a removal step; and the determination step just as required by the claims. Only routine skill would have been required to use an alternative yet functionally equivalent drug and labeled antibody in the method of determination as taught by de Jaeger et al., and Jehanli et al., since only the expected results would have been obtained. Baker et al., clearly teach that antibodies for the drugs are known in the art. Thus the use of alternative and functionally equivalent techniques would have been desirable to those of ordinary skill in the art based on the need to determine the presence of the drug and the availability of drugs, drug conjugates and associated antibodies. Therefore, applicants' arguments are not persuasive and the rejection is maintained.

Conclusion

6. No claims allowed.

7. Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

8. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Ja-Na Hines whose telephone number is 571-272-0859. The examiner can normally be reached on Monday-Thursday and alternate Fridays.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Lynette Smith can be reached on 571-272-0864. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Ja-Na Hines
January 26, 2006

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